

FIELD EVALUATION OF AN ORF VACCINE IN SHEEP AND GOAT FLOCKS WITH HIGH NEONATAL MORTALITY*
PROCENA ORF VAKCINE NA TERENU KOD STADA OVACA I KOZA SA VISOKOM NEONATALNOM SMRTNOŠĆU

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A high percent of annual neonatal mortality attributed to orf infection was observed between 2001 and 2004 in 2 sheep and 2 mixed (sheep and goat) flocks of Northern Greece. In order to protect the neonatal lambs and kids from orf infection a commercially available live orf vaccine was used. Pregnant sheep and goats were vaccinated subcutaneously a month before parturition, while 10 sheep and 10 goats in each flock remained unvaccinated and were used as negative controls. The vaccine was significantly effective ($P < 0.05$) in reducing the orf lesions and the mortality rate in lambs and kids of the 4 flocks. During the next year 3 of the 4 flocks were revaccinated. A significantly low percentage of orf lesions and neonatal mortality continued to occur in revaccinated flocks, while a significant percentage ($P < 0.05$) of orf lesions and neonatal mortality reappeared in the nonrevaccinated flock. The antibody titres in vaccinated sheep and goats were increased significantly on days 60 and 105 post-vaccination, while the titres in the controls remained low ($P < 0.05$).

Key words: lambs, kids, mortality, protection, orf, live vaccine

Introduction / Uvod

Contagious ecthyma (synonyms: contagious pustular dermatitis, orf, contagious pustular stomatitis, malignant aphtha, sore mouth, scabby mouth) is

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an infectious viral disease affecting mainly sheep and goats, but also reindeer and musk oxen. Experimental infection has been achieved in cattle, rabbits, horses and monkeys (Michelsen PGE, 2002). The orf virus is a zoonotic pathogen, as humans are also susceptible to orf, which is an occupational hazard of those that handle sheep and goats (Robinson AJ, Balassu TC, 1981). It has worldwide prevalence and causes noticeable economic effect through loss of condition, mastitis, abandonment and related deaths (Scott DW *et al.*, 1984; Scott DW, 1988), although in some cases the disease can have no economic impact (McElroy MC and Bassett HF, 2007).

The orf causative agent is a DNA epitheliotropic *Parapoxvirus* (family *Poxviridae*) virus. Genetic heterogeneity of the orf virus isolates circulate in different geographic regions as concluded from several molecular studies (Mazur C *et al.*, 2000; Kottaridi C *et al.*, 2006). The orf virus infects damaged or scarified skin and replicates in regenerating epidermal keratinocytes (McKeever DJ *et al.*, 1988; Haig DM and McInnes CJ, 2002; Haig DM *et al.*, 2002). The clinical progression of the infection is erythema, papule, vesicle, pustule and scab. The virus is shed with the scab to seed the environmental pool, where it survives for a long time (Reid HW, 2002). Transmission occurs through direct and indirect (fomite) contact (Scott DW *et al.*, 1984).

In sheep and goats, the disease usually occurs in young animals 3-6 months old, although neonatal lambs and kids aged 10-12 days old can be severely affected as well. In naive flocks the disease can affect also adult animals (Radostits OM *et al.*, 2000; Navarre CB *et al.*, 2002). Clinical signs include papules, vesicles, pustules and scabs. The lesions usually heal in 2-4 weeks (Scott DW *et al.*, 1984; Smith MC and Sherman DM, 1994; Reid HW, 2002). In lambs they are distributed around the mouth and nostrils, along the gums and in the oral cavity, on the thigh, axilla, poll, genitalia, lower limbs, coronet and ewe udder (Reid HW, 2002). In kids the lesions are distributed on the lips, muzzle, eyelids, oral cavity, udder, teats and feet (Scott DW., 1988). Affected animals usually exhibit a decrease in feed consumption and some become depressed, anorectic and febrile (Scott DW *et al.*, 1984; Scott DW, 1988). Complications of contagious ecthyma include secondary bacterial infections (respiratory, gastrointestinal, integumentary), myiasis, mastitis and lameness (Scott DW *et al.*, 1984; Scott DW., 1988; Anderson DE *et al.*, 2002). The morbidity can reach up to 100 % and the case fatality rate usually ranges between 5-15 %, although case fatality rates, up to 75 % (Radostits OM *et al.*, 2000) and mortality up to 78 % (Darbyshire JH, 1961) have been reported.

The host immune response controlling orf virus replication in the skin of infected animals is based on CD4 (+) T-cells and orf-virus-specific antibodies (McKeever DJ and Reid HD, 1987; McKeever DJ *et al.*, 1987; Lloyd JB *et al.*, 2000). Since the orf virus can produce a series of immune-modulator and virulence proteins, the host immune response is not effective to eliminate the virus rapidly (Haig DM, 2006). In primary infections, the virus is able to replicate for a period of time

before the host can mount an effective immune response. On the contrary, in re-infections, the immune memory response ensures a rapid accumulation of host immune effector molecules and the virus is contained and eliminated more rapidly than in primary infections (Haig DM and McInnes CJ, 2002). Nevertheless, re-infections are frequent.

Mild infections are usually self-limiting (Clarckson MJ, Faull WB, 1990; Michelsen PGE, 2002). In more severe infections various treatments have been applied, but results generally were not satisfactory (Reeid HW, 2002). Therefore, a great interest exists for disease prevention. Only live vaccines are recommended. The traditional vaccine virus is prepared from the infected scabs of orf virus lesions in sheep and is used to vaccinate animals by scratching with an applicator. Up to date, several studies were conducted to evaluate the efficacy of live vaccines against orf in sheep. However, there is a lack of accord between the researchers about their efficacy (Valder WA *et al.*, 1979; Mayr A *et al.*, 1981; Buddle BM and Pulford HD, 1984; Buddle, BM *et al.*, 1984; Pye D, 1990; Nettleton PF *et al.*, 1996). From these studies, only some (Mayr A *et al.*, 1981) have conducted a field trial, while all the other trials have been conducted in controlled conditions. The majority of these efficacy trials have been accomplished in sheep, while data for goat vaccination is very limited in literature.

Considering all the above information, the aim of this study was to assess the protection ability of a commercially available live vaccine, under field conditions in 4 small ruminant flocks in Greece, that had high lamb and kid mortality attributed to severe orf infections.

Materials and methods / Materijal i metode rada

Animals / Životinje

The main experimental study was conducted in 4 flocks of northern Greece (Macedonia and Thrace) in the year 2005. The next year, 2006, the same 4 flocks were monitored for their health status and the vaccine clinical efficacy.

Flock 1. consisted of Lacaune sheep and was reared in Kozani area of West Macedonia. Flock 2. consisted of Lacaune and Friesian sheep and was reared in Xanthi area (Thrace). Flock 3. was mixed and consisted of Chios sheep (purebred and crosses with other local dairy breeds) and goats of local dairy breeds; the flock was reared in the Kavala area (East Macedonia). Flock 4. was also mixed and consisted of purebred Chios sheep and goats of local dairy breeds; this flock was reared in the Thessaloniki area (Central Macedonia).

During the past years (2001-2004) high neonatal mortality, attributed to contagious ecthyma has been recorded in all flocks, as was confirmed by clinical examination, histopathology and PCR.

The animals of the 4 flocks were reared under a closed intensive feeding system. The adults were fed alfalfa hay, straw and a commercial concentrated feed according to their dietary requirements (NRC, 1981; 1985). The neonatal

lambs and kids were suckling their mothers and had free access to alfalfa hay and commercial concentrated feed. All the animals were free of ectoparasites, regularly dewormed and vaccinated against clostridial infections.

Vaccine / Vakcina

The vaccine Ecthybel[®], a product of Merial-France was used for this study. It contains live ecthyma virus cultured in cells at least 2.5×10^4 PFU.

Experimental design / Plan eksperimenta

In order to achieve homogenous crops of lambs and kids all ewes and does were estrus synchronized in June 2004. Each adult animal was also ear-tagged and at 2.5 months of pregnancy was examined by ultrasonography for their pregnancy status. In each flock, a month before the expected date of parturition (Day 0), all pregnant sheep and goats of each flock were separated from the non-pregnant animals.

From each participated flock, 10 sheep and 10 goats were randomly selected (a total of 40 sheep and 20 goats) as unvaccinated controls. From these animals blood samples were taken by jugular vein puncture and then they received a 1 ml subcutaneous injection of 0.9 % saline solution (Group 1 – control). The remaining pregnant sheep (1060 totally) and goats (130 totally) in each flock were vaccinated subcutaneously against orf virus (Group 2) with 1 ml of a commercial live vaccine (Ecthybel[®]) according to the vaccine instructions. Before vaccination blood samples were taken from 10 sheep and 10 goats randomly selected in each flock (40 sheep and 20 goats totally). After grouping, the animals of the 2 groups remained separate and were monitored daily for their health status. After parturition, their neonatal lambs and kids were also monitored daily. Lambs or kids with orf lesions were treated and the dead ones were immediately necropsied to identify the cause of death. Blood samples were also taken on days 60 and 105 post-vaccination from the adult animals.

The next lambing season (2006) the flocks 2, 3 and 4 were revaccinated as previously, while the owner of flock 1 refused to vaccinate his animals. The neonatal lambs and kids of the 2 groups were attended for their health status for 2 months.

Antibody determination / Određivanje koncentracije antitela

The blood samples were centrifuged at 3000 rpm for 20 min and the serum was kept at 4 °C. A commercial ELISA kit (Teqlab Rothe- Swizerland) based on a specific antigen was used and the serum was tested in four subsequent ten-fold dilutions. The samples were examined in duplicate for flock 2. One sample series was examined in the Laboratory of Microbiology and Infectious Diseases of the Veterinary School of Thessaloniki-Greece and the other in the Veterinary School of Hannover-Germany. For the other 3 flocks the samples were examined only in Thessaloniki.

Statistical analysis / Statističke analize

Data were stored in a database and analyzed using SPSS 10.0 software (SPSS, 2000). The statistically significant association was determined by the Chi-squared test and the level of significance was $P < 0.05$. In cases where the Chi-squared test was not applicable (expected frequency less than 1 and over 20% of expected frequencies less than 5), Fisher's exact test was applied.

Results / Rezultati

The vaccine efficacy assessment was based on the number of newborn lambs and kids of the 2 groups (vaccinated and controls) with orf lesions, on the neonatal mortality rate and on blood serum antibody levels of vaccinated and unvaccinated ewes and does.

The vaccine was significantly effective ($P < 0.05$) in reducing the orf lesions and the mortality in lambs and kids of the 4 flocks in total.

Flock 1. Fifteen out of 15 lambs (100 %) from unvaccinated mothers (Group 1) had orf lesions at the age of 10-20 days and they all died despite treatment. In dead lambs severe stomatitis and bronchopneumonia was observed at necropsy. On the contrary, all the lambs (210 out of 210-100 %) of group 2 remained healthy and no losses due to orf were recorded. *Flock 2.* Ten out of 20 lambs (50 %) from unvaccinated mothers (Group 1) had orf lesions when they were 10-12 days old and they died despite treatment. At necropsy the same lesions as in lambs of flock 1 were observed. Five out of the 10 (25 %) other lambs of Group 1 showed orf lesions and after treatment they survived, while the other 5 lambs (25 %) had no orf lesions and grow normally. Regarding Group 2 animals, only 6 out of 230 lambs (2.6 %) had mild orf lesions at the commissures of the lips and no deaths were recorded. *Flock 3.* All the lambs (18 out of 18-100 %) and kids (15 out of 15-100 %) from unvaccinated mothers (Group 1) had orf lesions at the age of 10-15 days and they died despite treatment. At necropsy severe stomatitis and bronchopneumonia were also observed. Mild orf lesions at the lips were observed in only 3 out of 700 (0.43 %) lambs of Group 2 and they were treated successfully, while neither orf lesions nor deaths were found in kids (65 out of 65-100 %) from vaccinated does. *Flock 4.* All the lambs (19 out of 19-100 %) and kids (19 out of 19-100 %) from unvaccinated mothers (Group 1) had orf lesions when they were 15 days old and all were treated. After treatment only 1 out of 19 lambs survived (5.26 %), while all the kids died despite treatment. At necropsy they were found to have severe stomatitis and bronchopneumonia. All the lambs (290 out of 290-100 %) and kids (160 out of 160-100 %) of Group 2 were fully protected. No orf lesions and mortality attributed to the orf virus were recorded.

The 2nd year (2006), the flocks 2, 3 and 4 that were revaccinated 1 month before parturition had minimal losses due to orf infection. The 1st flock that was not revaccinated had orf lesions in 80 % of the neonatal lambs and mortality in 51.74 % of neonatal lambs (150 out of 290). The deaths were attributed to severe

stomatitis and bronchopneumonia. The morbidity and mortality rate in unvaccinated flock 1 were significantly higher compared with the previous year ($P < 0.05$).

No difference in antibody titres was recorded in the serological examination between the 2 laboratories. On Day 0 there were no significant differences in mean antibody titres ($P > 0.05$) of the animals in the 2 groups. Besides, there were no significant differences in mean antibody titres of unvaccinated sheep and goats (Group 1) on days 0, 60 and 105 ($P > 0.05$). A statistically significant increase ($P < 0.05$) in mean antibody titres of sheep and goats among the 3 samplings (105 day > 60 day > 0 day) of the vaccinated Group 2 was recorded. The antibody titres in animals of Group 2 were significantly higher ($P < 0.05$) than in Group 1 on days 60 and 105.

The number of the animals of each flock and the losses of the previous year (2004), before the experiment, are shown in Table 1. The mortality rates for vaccinated and non-vaccinated flocks are shown in Table 2. Figure 1 shows the results of serological examination from sheep of flock 2.

Table 1. Number of animals and losses in the 4 flocks for the year 2004 /

Tabela 1. Broj životinja i gubici kod 4 stada tokom 2004.

Flock No / Stado broj	Adult animals / Odrasle životinje		Neonates / Neonatalne životinje		Dead / Uginule		Alive / Žive	
	Ewes / Ovce	Does / Koze	Lambs / Jagnjad	Kids / Jarad	Lambs / Jagnjad	Kids / Jarad	Lambs / Jagnjad	Kids / Jarad
1	200	-	300	-	297	-	3	-
2	200	-	290	-	275	-	15	-
3	500	50	750	95	220	30	530	65
4	200	100	290	200	150	50	140	150

Table 2. Lamb and kid mortality rate for vaccinated and non-vaccinated (control) sheep and goat flocks /

Tabela 2. Stopa smrtnosti jagnjadi i jaradi kod vakcinisanih i nevakcinisanih (kontrolnih) stada ovaca i koza

Flock No / Stado broj	Vaccinated sheep / Vakcinisane ovce	Control sheep / Kontrolne ovce	Vaccinated goats / Vakcinisane koze	Control goats / Kontrolne koze
1	0 %	100 %	-	-
2	0 %	50 %	-	-
3	0 %	100 %	0 %	100 %
4	0 %	94.74 %	0 %	100 %

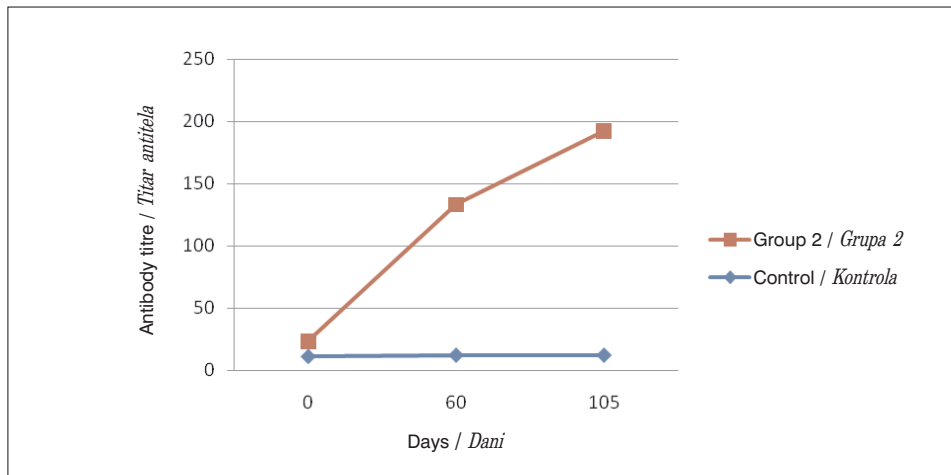


Figure 1. Antibody titres in sheep of the 2 groups on days 0, 60 and 105 /
Slika 1. Titri antitela kod ovaca grupe 2 na dane 0, 60 i 105

Discussion / Diskusija

Although a number of proprietary treatments as well as homeopathic preparations are available, the treatment of orf infections is usually not effective (Reid HW, 2002). Moreover, the possible beneficial effects of treatment must be weighed against the danger of zoonotic infection (Valder WA *et al.*, 1979; Smith MC and Sherman DM, 1994). Therefore, prevention measures of applying effective vaccination programs was essential, especially in flocks which experienced a high neonatal mortality rate in the previous years despite the application of different treatment protocols.

The use of orf vaccines in the field had a long story with controversial aspects about their efficacy and safety. Although they can limit the severity of the disease, they are not completely effective and vaccine strains may be the source of outbreaks (Girly JA *et al.*, 1998). Nevertheless, their use is considered necessary especially in cases with a high neonatal mortality rate, as has been shown in the 4 flocks referred to in this study. Since there are no commercial vaccines against orf virus licenced in the Greek market, a special licence was obtained from the Ministry of Agriculture for the use of Ecthybel[®] that is available in France. In literature, no available scientific information was found regarding the efficacy of this commercial vaccine in the field, something that probably makes this trial more interesting.

According to the vaccine instructions, pregnant animals should be vaccinated one month before parturition. Otherwise, neonatal lambs or kids should be vaccinated after the onset of the symptoms of the disease. In the pres-

ent study, it was decided to vaccinate only adult animals, because results of a previous preliminary study conducted in Greece (Giadinis N, 2006) indicated that vaccination of neonatal lambs and kids with Ecthybel[®] was not effective.

Several trials for the evaluation of different orf vaccines had contradictory results. Different routes of vaccine administration and only sheep of different age and productive stage were used. Information regarding orf vaccination in goats is limited. In fact, only one trial so far has been reported in Norway. Unfortunately, the results of this trial were not reliable, as there was a contamination of the vaccine with the Border disease virus (Loken T *et al.*, 1991). The results from our study could be the first field trial with orf vaccine in goats.

In the present study, pregnant sheep and goats were vaccinated 1 month before parturition. The vaccine was administered with subcutaneous injection, which is an easy way of administration and is the common route of administration for the majority of small ruminant vaccines (Mobini S *et al.*, 2002). The subcutaneous route to vaccinate sheep against orf has been used only by some authors (Mayr *et al.*, 1981), while skin scarification of the inner thigh or the axilla is the most preferable route of orf vaccine administration (Buddle BM and Pulford HD, 1984; Buddle BM, 1984; Scott DW, 1988; Clarckson MJ and Faull WB, 1990; Pye D, 1990; Nettleton PF *et al.*, 1996). Regarding the age and productive stage of vaccinated animals, many researchers in order to achieve better efficacy preferred to vaccinate lambs and not adult animals (Buddle BM and Pulford HD, 1984; Buddle BM, 1984; Nettleton PF *et al.*, 1996). Vaccination with the Scabivax[®] (Coopers Pitman-Moore) was more effective when administered in lambs or in the early or mid-gestation period of ewes (Clarckson MJ and Faull WB, 1990). In our study, the vaccine administration 1 month before parturition to ewes and does was effective without side effects. Our results are in accordance with the findings of Mayr A *et al.* (1981), who vaccinated 4 sheep flocks with high lamb morbidity and mortality due to orf infection. They found, that sheep vaccination in late pregnancy reduced significantly morbidity and minimized almost totally the neonatal mortality. Lamb vaccination in the later study was also effective, but not as effective as in the vaccination of pregnant sheep.

The efficacy of vaccination in other trials differed. In Germany, Mayr A *et al.* (1981) had similar problems in sheep flocks with high morbidity and mortality and the live vaccine they used was also effective. Buddle *et al.* (1984) and Buddle and Pulford (1984) had also good efficacy by vaccinating lambs, but had no efficacy by vaccinating pregnant ewes. Nettleton *et al.* (1996) used a commercial vaccine that was very effective in lambs, as in vaccinated lambs the lesions were milder than in unvaccinated ones. In literature, there were no studies reported about the efficacy of the orf vaccine in goats. As it has been shown in our study, the vaccination of pregnant does 1 month before parturition gives good protection to neonatal kids, as they had a low morbidity and mortality rate compared with non-vaccinated controls.

Michelsen (2002) considered that vaccination failures can be attributed to the different strain virulence, but Reid HW (2002) assessed that there was no evidence to suggest that field isolates of different virulence existed. Pye (1990) had different results in Australia vaccinating sheep with 2 different vaccine strains (effective, non-effective).

In literature, vaccination failures for the orf virus are not attributed to the antigenic difference between the vaccine and field strains (Buddle BM, Pulford HD, 1990; Nettleton PF *et al.*, 1996; Michelsen PGE, 2002). According to Nettleton PF *et al.* (1996) a live orf vaccine with an Australian strain had very good efficacy against the British strains. Our results are also confirmatory, since the French vaccine strain of Echthel was very effective in protecting the animals of 4 flocks in different areas of northern Greece.

The vaccine was clinically effective in reducing the morbidity and mortality rates in lambs and kids, while the orf lesions were milder in lambs and kids of vaccinated mothers. The clinical efficacy of the vaccine was further confirmed by the 2nd year of the study, because the owner of flock 1 refused to vaccinate his flock, while the owners of the other flocks vaccinated them. There was an increased morbidity and mortality rate in flock 1 compared with the previous year (when he had vaccinated the animals) and the other 3 flocks, that continued to have reduced morbidity and mortality due to vaccination. Since the immunity is not long lasting (McKeever DJ and Reid HD, 1987) and reinfections are frequent, revaccination appears necessary.

In the present study, antibody levels determination by the ELISA test in sheep and goats showed an increase after vaccination. The same results have also been found in other studies with ELISA (Buddle BM, Pulford HD, 1990; Nettleton PF *et al.*, 1996). Yirell *et al.* (1989) vaccinated SPF Suffolk crossbred lambs and found an increase in antibody titres post-vaccination using ELISA, although some animals did not respond. The humoral response is affected by several factors; one of them is the animal breed (McKeever DJ *et al.*, 1987). In other studies, an increase on post-vaccination titres was also found with other methods as the virus neutralization test (VN) and microtitre plate system (Mayr A *et al.*, 1981; Buddle BM *et al.*, 1984; Pye D, 1990). As it has been shown by Housawi FMT *et al.* (1992), ELISA is superior to AGID and CFT for orf antibody detection. However, in orf infections antibody determination is not indicative of the degree of protection from the disease (Buddle BM and Pulford HD, 1984; McKeever DJ *et al.*, 1987), because the cellular immune response and related immunomodulatory factors play a primary part in the protection from orf infection (McKeever DJ *et al.*, 1987; Haig DM *et al.*, 2002). So, post-vaccination antibody titres for the orf virus could be a good indicator for previous exposure to the virus, as was the vaccination with a live vaccine, but not for protection from the disease (Nettleton PF *et al.*, 1996).

From this study, it could be concluded, that vaccination of pregnant sheep and goats during the last month of gestation with a live orf vaccine (Echthel

bel®-Merial) appears to give good protection to neonatal lambs and kids against orf virus infection. However, annual re-vaccination seems to be necessary.

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ENGLISH

PROCENA ORF VAKCINE NA TERENU KOD STADA OVACA I KOZA SA VISOKOM NEONATALNOM SMRTNOŠĆU

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Visok stepen godišnje smrtnosti neonatalnih životinja doprineo je orf infekcijama uočnim između 2001 i 2004 kod dva stada ovaca i dva mešovita stada ovaca i koza u severnoj Grčkoj. Komercijalno dostupna živa orf vakcina je upotrebljena da bi se zaštitila neonatalna jagnjad i jarad od orf infekcije. Bređe ovce i koze su vakcinisane subkutano mesec dana pre partusa, dok je 10 ovaca i 10 koza u svakom stadu ostalo nevakcinisano i poslužile su kao negativne kontrole. Vakcina je bila značajno efikasna ($P < 0,05$) u smanjenju orf lezija i stope smrtnosti kod jagnjadi i jaradi sva četiri stada. Tokom sledeće godine, 3 od 4 stada su revakcinisana. Nastavljena je pojava značajno niskog procenta orf lezija i smrtnosti neonatalnih životinja u revakcinisanim stadima, dok se ponovo pojavio značajan procenat ($P < 0,05$) orf lezija i smrtnosti neonatalnih životinja kod stada koja nisu revakcinisana. Titri antitela kod vakcinisanih ovaca i koza su bili značajno povišeni 60 i 105 dana posle vakcinacije, dok su titri kod kontrola ostali niski ($P < 0,05$).

Ključne reci: jagnjad, jarad, smrtnost, zaštita, orf, živa vakcina

РУССКИЙ

ОЦЕНКА ОРФ ВАКЦИНЫ НА МЕСТЕ У ОТАРЫ ОВЕЦ И КОЗ С ВЫСОКОЙ НОВОРОЖДЁННОЙ СМЕРТНОСТЬЮ

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Высокая степень годовой смертности новорождённых животных содействовал орф инфекциям замеченным между 2001 и 2004 у двух отар овец и двух смешанных отар овец и коз в северной Греции. Коммерчески доступная живая орф

вакцина употреблена, чтобы охранились новорождённые ягнята и козлята от орф инфекции. Беременные овцы и козы вакцинированы подкожно месяц тому назад до родов, пока 10 овец и 10 коз в каждой отаре остались невакцинированы и воспользовались как отрицательные контроли. Вакцина была значительно эффективная ($P<0,05$) в уменьшении орф повреждений и ставки смертности у ягнят и козлят всех четырёх отар. В течение следующего года, 3 и 4 отар ревакцинированы. Продолжено явление значительно низкого процента орф повреждений и смертности новорождённых животных в ревакцинированных отарах, пока снова появился значительный процент ($P<0,05$) орф повреждений и смертности новорождённых животных у отар, которые не ревакцинированы. Титры антител у вакцинированных овец и коз были значительно увеличены 60 и 105 дней после вакцинации, пока титры у контролей остались низкие ($P<0,05$).

Ключевые слова: ягнята, козлята, смертность, охрана, орф, живая вакцина